Leptin and Nitric Oxide Production Against Ischemic Neuronal Injury

To the Editor:

We read with great interest the article by Dr Zhang and colleagues1 dealing with neuroprotective effects of leptin against ischemic injury in the brain. The results of their study demonstrated that leptin significantly protected primary cortical neurons against death induced by oxygen-glucose deprivation in cultured rat cortical neurons. The authors also indicated that intraperitoneal administration of leptin dose-dependently reduced infarct volume induced by middle cerebral artery occlusion in the mouse brain. The authors proposed that leptin might be neuroprotective against ischemic neuronal injury, and that the extracellular signal-related kinase (ERK) 1/2 signaling pathway could play a critical role in leptin-mediated neuroprotection.

Recently, it has been shown that nitric oxide (NO) may actively participate in neuroprotection and neurogenesis in cerebral ischemia. Khan et al2 demonstrated the cerebrovascular protective efficacy of various NO donors in rats after experimental stroke. Evidence indicates that leptin has an important role in the regulation of NO production. It was shown that leptin attenuated cardiac contraction in rat ventricular myocytes, possibly through an increased NO production.3 In a study we presented previously, a relationship between membrane fluidity (a reciprocal value of membrane microviscosity) of erythrocytes and leptin was investigated by means of an electron paramagnetic resonance method.4 The decreased membrane fluidity of erythrocytes might cause a disturbance in the blood rheologic behavior and the microcirculation, which could contribute, at least in part, to the pathophysiology of circulatory disorders. We demonstrated that leptin increased the membrane fluidity of erythrocytes and improved the rigidity of cell membranes in humans via the NO- and cGMP-dependent mechanism.4 One hypothesis is that leptin may actively participate in the improvement of the rheologic behavior of erythrocytes and the microcirculation by increasing NO production, which would be a defense against vascular complications in circulatory disorders. In the separate series of the study, we also showed that the relaxing effect of leptin on blood vessels was partially mediated by the NO-dependent pathway.5 In this context, we speculate that leptin-induced NO could have a crucial role in the neuroprotective effect against ischemic neuronal injury. Therefore, we would like to know whether NO signaling might be related to the leptin-effect in the study of Dr Zhang and colleagues. It would be necessary to assess more precisely the functional interactions between leptin and NO, and their contribution to the treatment of ischemic stroke.

Disclosures

None.

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*Stroke*. 2008;39:e3; originally published online December 6, 2007;
doi: 10.1161/STROKEAHA.107.500892
*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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